

Technical Abstract (Original Protocol)

Leukocyte adherence deficiency (LAD) is a congenital immunodeficiency disorder characterized by defects in neutrophil function which results in recurrent, life-threatening bacterial infections in affected individuals. LAD results from single gene defects in the leukocyte integrin beta subunit, CD18, a necessary partner for cell surface expression of the CD11 subunits.

The purpose of this study is to investigate whether ex-vivo retrovirus-mediated gene transfer of the cDNA for the human leukocyte integrin CD18 subunit followed by infusion of transduced cells into the patient is safe and able to improve or cure the disease. Peripheral blood repopulating cells will be mobilized by treatment of the patient with recombinant human granulocyte-colony stimulating factor, collected by leukapheresis, and selected for CD34+ positive cells by avidin-biotin immunoabsorption. CD34 positive cells will then be transduced ex vivo over a 3 day period in flasks coated with recombinant fibronectin fragment and containing medium with retrovirus supernatant and growth factors. After transduction, cells will be re-infused into the patient without myeloablative treatment. Collection, transduction and infusion of the transduced peripheral blood repopulating cells will be repeated four times at one-month intervals to increase the amount of transduced repopulating cells.

The primary endpoint of this study is to examine the safety of infusing peripheral blood repopulating cells transduced with the human CD18 cDNA. The persistence and expression of the CD18 gene in hematopoietic cells after infusion will also be studied.